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Response to Paper No.	:	13

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TRAVERSAL AND REQUEST FOR RECONSIDERATION OF REQUIREMENT FOR RESTRICTION

Sir:

Applicants, through their undersigned attorneys, hereby traverse the requirement for restriction set forth in an Official Action mailed on March 19, 2001 in the above-identified patent application. The Examiner contends that the originally filed claims were directed to three (3) distinct inventions, as follows:

Group I, claims 1 to 3 and 24 to 39, directed to hybrid PKS genes, vectors thereof, transformed organisms thereof, methods of making said transformed organisms, and hybrid PKS enzymes;

Group II, claim 40, drawn to polyketides; and

Group III, claims 41 to 43, drawn to type II PKS promoters linked to heterologous genes.

Applicants respectfully maintain that the restriction requirement set forth above is improper for failure to comply with the relevant provisions of the Manual of Patent Examining Procedure (M.P.E.P.) pertaining to restriction requirements.

The present application was filed under 35 U.S.C. §371 as a U.S. national stage application under the Patent Cooperation Treaty.

As stated in § 1893.03(d) of the M.P.E.P.:

> Examiners are reminded that unity of invention (not restriction) practice is applicable in international applications (both Chapter I and II) and in national stage (filed under 35 U.S.C. 371) applications...
>
> The principles of unity of invention are used to determine the types of claimed subject matter and the combinations of claims to different categories of invention that are permitted to be included in a single international or national stage patent application. The basic principle is that an application should relate to only one invention or, if there is more than one invention, that applicant would have a right to include in a single application only those inventions which are so linked as to form a single general inventive concept.
>
> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art.... Note also examples 1-17 of Annex B Part 2 of the PCT Administrative

Instructions as amended 01 July 1992
contained in Appendix AI of the M.P.E.P.

In Example 17, it is clearly stated that there are corresponding special technical features between a protein and the DNA sequence encoding the protein, and therefore there is also unity of invention between them.

Moreover, it is noteworthy that, during the international stage of this application, in the International Search Report published on January 15, 1998, the Examiner found a lack of unity between two (2), not three (3), groups of claims. These were as follows:

Group I, claims 1 to 19, drawn to hybrid polyketide synthase gene, hybrid polyketide synthase thereby encoded, vector and transformed organism containing said gene, method of producing such a transformed organism, use thereof for making a polyketide, **and polyketide so obtained**; and

Group II, claims 20 to 23, drawn to use of a type II PKS promoter to control a heterologous gene and nucleic acid comprising a type II PKS promoter operably linked to a heterologous gene. [*Emphasis supplied.*]

Plainly, the present restriction requirement fails to comply with the established United States Patent and Trademark Office practice of following the international rules regarding unity of invention in the prosecution of applications filed under § 371.

Second, even if standard restriction practice were applicable in this case, it is improper to require restriction between the nucleotide sequences in the present application and the proteins they encode, *i.e.*, between Groups I and II.

According to 35 U.S.C. 121, "If two or more **independent and distinct** inventions are claimed in one application, the

Commissioner may require the application to be restricted to one of the inventions." [*Emphasis supplied.*] It is well established, however, that the sequence of nucleotides in a gene determines the order of the amino acids in the proteins encoded by the genes. According to M.P.E.P. § 802.01,

> The term "independent" (i.e., not dependent) means that there is no disclosed relationship between the two or more subjects disclosed, that is, they are **unconnected** in design, operation, or effect...

[*Emphasis supplied.*] Since the order of the nucleotides in a gene and the order of amino acids in the corresponding protein are, in fact, intimately connected, the inventions of Groups I and II are not independent.

Therefore, even under restriction practice as it applies to applications filed under 35 U.S.C § 111(a), for example, restriction should not have been required between the claims directed to hybrid polyketide synthase encoding nucleic acids and polyketides encoded thereby.

Plainly, the above-captioned restriction requirement fails to comply with the established United States Patent and Trademark Office practice of following the international rules regarding unity of invention in the prosecution of applications filed under § 371. Moreover, the present requirement also fails to comply with established restriction practice as it applies to applications filed under 35 U.S.C § 111(a). Applicants, therefore, respectfully traverse the restriction requirement and request that it be withdrawn upon reconsideration.

In order to be fully responsive to the above-mentioned requirement, Applicants elect the subject matter of Group I for consideration in this application, namely, the subject matter of claims 1 to 3 and 24 to 39, directed to hybrid PKS genes, vectors thereof, transformed organisms thereof, methods of making said transformed organisms, and hybrid PKS enzymes.

Applicants hereby reserve the right to file one or more continuing applications, as provided in 35 U.S.C. §120, on the subject matter of any claims finally held withdrawn from consideration in this application.

Applicants thank the Examiner for the Comments appended to the Official Action of March 19, 2001. In response, Applicants offer the following remarks and clarifications.

With respect to Claim 24, Applicants note that this claim refers to a gene having a "first nucleic acid portion" which "encodes a loading module together with the ketosynthase ("KS") domain of the homologous extender molecule." The "first nucleic acid portion" encodes part of a type I PKS, as stated in claim 1. Claim 2 further defines this part as including at least the loading module, and claim 24 still further defines this part as including the KS of the extender module that is "homologous," that is, the KS that would naturally be associated with the extender module. There would not be an extender on the upstream side of the loading module. In terms of the DEBS system such a hybrid gene would comprise AT-ACP-KS.

With respect to claim 28, the terminology of "combinatorial modules" is explained in the specification on page 9 in the final paragraph, especially at lines 25 to 27. In general, Applicants are not concerned with duplicated gene regions as the splice sites with be in corresponding conserved marginal regions or linker regions between domains near known sites for limited proteolysis. Applicants note that, instead of producing hybrids by exchanging "natural modules," the portion of DNA to be exchanged may include the contents of one or more modules. The portion to be exchanged, however, may span the end part of one "natural module" and the beginning part of a following "natural module." Applicants also note that the "following natural module" may be a later one than the one which follows consecutively.

Concerning claim 30, Applicants have no clarification to offer at this time and, accordingly, it is respectfully requested that this claim be examined as it was originally filed.

Early and favorable action on the merits of this application is respectfully solicited.

Respectfully submitted,

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